REMARKS

Claim 50 has been amended to insert the definition of the variable, "q". Support for this amendment is found on page 8, line 19 of the specification. Claims 44 and 45 have been amended to conform to each other. Claim 46 has been amended to clarify that the pharmaceutical is administered to the host.

Election/Restriction

Since no prior art was found, the search and examination should be expanded to include methods which employ the compounds defined in claims 51 and 59-74. In addition, the search and examination should be expanded to include the diseases recited in claims 57 and 58.

Additionally, the examination should be expanded to include the subject matter which was previously elected, searched, examined and allowed in this application prior to filing the RCE. The independent compound claims (claims 26 and 39) were allowed prior to filing the RCE. Claim 44 defines a subgenus of compounds within the scope of previously allowed claim 26 and claim 45 defines compositions prepared from these compounds. It would not be an undue burden to extend the examination to this subject matter which is either encompassed by previously allowed claim 26 (claim 44) or incorporates the subject matter of previously allowed claim 26 (claim 45). No basis has been given to withdraw the allowance of these claims.

Applicants attorney regrets the error made in identifying the claims which correspond to the elected subject matter in the response filed on May 20, 2004. Claim 36 was erroneously identified as corresponding to the elected subject matter when method claim 46 should have identified instead. Claim 46 depends on claim 26, which recites the elected species, "N-(4-tert-butylpyridinyl)-N'-(4-)4-methoxyphenoxy)phenyl) urea."

Priority

Although the elected species was not disclosed until the filing date of the instant application, this is not a proper basis for assigning a priority date of April 20, 2001, to the broad generic claims. No evidence has been presented that these broad generic claims are not supported by the parent applications.

Rejection Under 35 U.S.C. § 112, first paragraph

Applicants submit the Examiner has not provided sufficient evidence or adequate reasons to support the rejection under 35 U.S.C. § 112, first paragraph.

The specification provides a two pages of publications which have correlated TNFα production and MMP production with a number of diseases. Since inhibition of p38 leads to the inhibition of TNFα and MMP production, the p38 inhibitors of this invention will be useful in treating these diseases. No evidence has been presented to refute the findings or conclusions made in these publications or the present application. No evidence has been presented that any compounds of this invention, as inhibitors of p38, would not be effective in treating the diseases identified. Furthermore, no evidence has been presented of the allegedly "painstaking experimental study" necessary to use the invention commensurate in scope with the claims.

Only unsupported allegations and conclusions regarding the state of the art are provided to support the rejection such as, "there are no known compounds of similar structure which have been demonstrated to treat (i) all types of diseases that are mediated through p38 .." Applicants wish to draw the examiner's attention to US Patent No. 5,932,576, which contains claims to treating p38 mediated diseases using other small molecule compounds.

However, even if these allegations were true, they are irrelevant to enablement. As discussed in Wands, cited by the Examiner, "considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." No evidence has been presented that the specification is deficient in this regard.

In applying the factors set forth in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) the Examiner is requiring that the application meet clinical standards as set by the FDA to satisfy the enablement requirement under 35 U.S.C. § 112, first paragraph. For example, the Examiner requires proof that "inhibition of p38 leads to effective treatment of the claimed

disease conditions." The proof referred to by the Examiner is not necessary to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. As stated in *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995) with respect to the utility requirement,

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. *Scott*, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs will prevent any companies from obtaining patent protection on the promising new invention, thereby eliminating an incentive to pursue, through research and development, potential cures in any crucial area such as the treatment of cancer.

This rationale translates to prescribing the disclosure necessary to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph.

In any event, the specification provides ample guidance as to how to prepare pharmaceutical compositions with the compounds of this invention and how to administer these compositions in the treatment of the diseases identified. The specification also provides dosage ranges for the various methods of administration. Given the extent of the disclosure provided, it would at most involve routine experimentation if any at all, for one of ordinary skill in the art to treat any one of the recited diseases with a compound of this invention.

Even absent the specification disclosures discussed above, the rejection is clearly deficient in general under controlling case law. The courts have placed the burden upon the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated; see, e.g., *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971) (holding that how an enablement teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance.) The disclosure must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein. See *In re Marzocchi*, supra. No such evidence or reason for doubting Applicants' disclosure has been provided. Only general statements and conclusions are made.

Additionally, "the [enablement] requirement is satisfied if, given what they [, those of ordinary skill in the art,] already know, the specification teaches those in the art enough that

they can make and use the claimed invention without 'undue experimentation.'" See *Amgen v Hoechst Marion Roussel*, 314 F.2d 1313, 65 USPQ2d 1385 (Fed. Cir. 2003). Using the claimed compounds would be routine for those of ordinary skill in the art in view of applicant's disclosure. "An inventor need not ... explain every detail since he is speaking to those skilled in the art," *In re Howarth,* 654 F.2d 105, 210 U.S.P.Q. 689 (CCPA 1981). "Not every last detail is to be described, else patent specifications would turn into production specifications, which they were never intended to be," *In re Gay*, 309 F.2d 769, 774, 135 U.S.P.Q 311 (CCPA 1962).

There is no requirement that an applicant provide any working examples relating to the treatment of every claimed disease to satisfy the statute. See, for example, *In re Angstadt*, 537 F.2d at 502-03, 190 USPQ 214 (CCPA 1976) (deciding that applicants "are *not* required to disclose *every* species encompassed by their claims even in an unpredictable art"); *Utter v Higara*, 845 F.2d at 998-99, 6 USPQ2d 1714 (Fed. Cir. 1988) (holding that a specification may, within the meaning of Section 112, Para. 1, enable a broadly claimed invention without describing all species that claim encompasses). Instead, as discussed earlier, there is no requirement for any examples. See, for example, *Marzocchi*, supra, stating that how "an enabling teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance." The MPEP also agrees by stating that "compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." See MPEP § 2164.02.

The PTO has failed to meet its burden of establishing that the disclosure does not enable one skilled in the art to make and use the compounds recited in the claims. Instead of relying on proper probative evidence, the rejection is improperly based on bare allegations and conclusions. No evidence has been presented which would demonstrate that the guidance provided by the specification is inadequate to enable the use of the claimed compounds without undue experimentation.

Here, the specification provides more than it needs to, e.g, *in vitro* p38 kinase assays (and IC_{50} data) and *in vivo* assays. In similar fashion, one of ordinary skill in the art by performing the same or similar tests, can, by routine experimentation, determine the activity levels of each of the claimed compounds in treating various cancers. This is absolutely routine in the field.

Thus, appellants have provided more than adequate guidance (and examples) to enable the claimed invention.

For the reasons discussed above, Applicants submit that claims 74, 80, 81, 87 and 93 meet the requirements of 35 U.S.C. § 112, first paragraph.

Rejection Under 35 U.S.C. § 112, second paragraph

Applicants have inserted the definition of "q" found in the specification, which was inadvertently excluded from claim 50 when presented.

Double Patenting

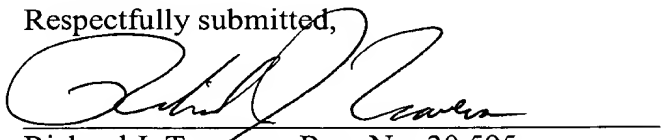
The claims in US application No. 10/361,858 are directed to distinct methods which target the VEGF-induced signal transduction pathway and not p38. Applicants acknowledge the compounds employed in each of these methods significantly overlap; however, the same compound can be used in patentably distinct methods. No evidence has been presented that the methods of these two applications are not patentably distinct when all limitations are considered, i.e., when the inventions are each considered as a whole.

Applicants have provided the "Notice of References Cited" for relevant copending applications in an IDS, which were crossed out as not considered. US Application No 10/086,417 claims the same priority as the present application. US Application Nos. 09/948,915, 09/889,227 and 10/042,226 claim the use of compounds which significantly overlap those employed in the instant invention in methods which inhibit raf kinase. US Application No. 10/848,567 claims the use of compounds which significantly overlap those employed in the instant invention in methods which inhibit PDGFR and other targets.

Applicants submit that all claims are in condition for allowance and that the broad generic claims are entitled to the priority claim. In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which can be expedited by a telephone conference, the examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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